Reply

Applicants wish to thank Examiner Carlson for the telephone interview and consideration of comments made by Applicants' counsel on July 3, 2002. Upon entry of the present amendment, claim 11 has been canceled without prejudice or disclaimer. Applicants reserve the right pursue the subject matter of all canceled claims in one or more divisional or continuation applications.

The title has been amended to more explicitly describe the presently claimed invention. Claims 37-58, 62-63, 67-68, 72-73 have been amended to impart proper antecedent basis and/or to specify that the claimed polypeptides are capable of being used to generate or select an antibody. Support for the amended claims can be found in the specification, for example, at: page 69, lines 35-37; page 71, lines 9-11; page 76, lines 17-23; and, page 79, line 21 to page 80, line 19. Claims 25-76 are currently pending. No new matter has been added.

Interview Summary of April 23, 2002

In regard to the interview summary issued for the April 23, 2002 telephonic interview (*see*, Paper No. 10) and comments pertaining to that interview in the present office action (*see*, Paper No. 11, page 2), Applicants wish to clarify for the record that Applicants agreed to limit the subject matter encompassed by claim 11 to SEQ ID NO:59 (wherein claim 11 recites SEQ ID NO:Y) only for the presently pending claims. Applicants reserve the right to pursue the full scope of the subject matter encompassed by claim 11 (i.e., wherein claim 11 recites SEQ ID NO:Y) in one or more subsequently filed divisional or continuation applications. However, claim 11 has herein been canceled without prejudice or disclaimer.

Claim Rejections Under 35 U.S.C. § 101

Claims 1 and 26-76 have been rejected under 35 U.S.C. § 101. *See*, Paper No. 11, page 2, last sentence.

The Office Action Summary (page 1) and comments on page 2 of the presently pending Office Action indicate that "Claims 1, 13, and 17-24 have been withdrawn from further consideration" and "Claims 11 and 25-76 are currently under examination." *See*, Paper No. 11. Therefore, Applicants presume that the Examiner intended the above cited rejection to apply to claims 11 and 25-76 (as opposed to claims 1 and 26-76 recited in Paper No. 11, at page 2, last sentence). Applicants response (below) is based on this presumption. Applicants respectfully request clarification if this presumption is incorrect.

Accordingly, Applicants understand that in the presently pending Office Action claims 11 and 25-76 were rejected as allegedly "not supported by either a specific or substantial asserted utility or a well established utility." *See*, Paper No. 11, page 2, last paragraph. In particular, it was asserted:

> [I]t is clear that the Fn14 or TWEAK receptor polypeptides are at least 90% identical to SEQ ID NO:59 and are variants or homologs thereof. In either event, or in all events, the action of Fn14 and of TWEAK receptor has been demonstrated, and these activities do not correspond to those activities surmised for SEQ ID NO:59 of the specification. Therefore, the teachings of Feng et al. and of Wiley support this rejection of the claims...

See, Paper No. 11, page 5, first full paragraph.

Applicants respectfully disagree with the above asserted conclusion.

As an initial matter Applicants note that, as of the present applications' priority filing date, it was well known by those of ordinary skill in the art that wound, tissue, organ and tumor vascularization occurs by a process called angiogenesis (i.e. angiogenesis is the process of endothelial cells invading a given "target" tissue to form new capillaries. *See, e.g., Alberts, et al.*, Molecular Biology of The Cell, 2nd Ed., page 964 (1989) ("New vessels always originate as capillaries, which sprout from existing small vessels. This process of angiogenesis occurs in response to specific signals...") (Copy of page 964 enclosed herewith). *Alberts et al.* also explains that vascularization is important in tumor growth. *Id.* at page 965, second paragraph ("To grow further, a tumor must induce

formation of a capillary network that invades the tumor mass.") (Copy of page 965 enclosed herewith). Hence, at the time of Applicants' priority date for the present application it was well-known by those of ordinary skill in the art that: 1) angiogenesis is a process wherein endothelial cells invade and vascularize new areas of tissue; and, 2) vascularization (or angiogenesis) is necessary for unhindered growth of tumors.

Further, Applicants submit that the teachings of the present specification have asserted specific and substantial utilities for the presently claimed polypeptides. For example, Applicants' specification teaches that the claimed polypeptides are useful for diagnosis of diseases and conditions which include vascular disorders and impaired wound healing. *See*, specification, page 24, lines 25-28. The specification further teaches that expression in endothelial cells indicates the product of this gene may be useful in the treatment and/or prevention of a variety of vascular disorders. *See*, specification, page 25, lines 17-20. The specification also teaches that protein products of this gene are useful in the treatment of wound healing deficiency, skin disorders, and integumentary tumors (e.g. various carcinomas and malignant melanoma). *See*, specification, page 25, lines 5-8. And, the specification teaches that protein, as well as antibodies directed against the protein, may show utility as a tumor marker and/or immunotherapy target. *See*, specification, page 25, lines 22-24. Furthermore, the specification also teaches that polypeptide variants, fragments, fusion proteins, and antibodies particularly constitute embodiments of the invention. *See, e.g.*, specification at: pages 72-77 (variants); pages 77-79 (fragments); pages 79-80 and 116-118 (antibodies); and, pages 80-81 and 115-116 (fusion proteins).

Additionally, the present specification particularly described Fc fusion proteins as important embodiments of the invention and also described how to make and use such fusion proteins (*see e.g.*, specification, at page 81, lines 15-26, and at pages 115-116). Furthermore, Applicants' specification also taught that antibodies and polypeptide receptors could be used as antagonists for inhibiting activity of target polypeptides. *See e.g.*, specification at page 94, line 35 to page 95, line 3. The present specification also particularly pointed out that assays used to identify antibodies and polypeptides with a desired binding activity could be useful "to treat disease or to bring about a particular result in a patient (e.g. blood vessel growth) by activating or inhibiting the polypeptide/molecule." *See*, specification, page 95, lines 32-35.

By comparison, the PCT publication by *Wiley* (WO01/45730A2) lends independent corroboration to Applicants description in the present specification. For example, like the Applicants' specification, *Wiley* teaches that the TWEAK receptor is expressed in endothelial cells. *Compare e.g., Wiley* at page 2, lines 27-28 *with* Applicants' specification at page 24, lines 23-24. Also like the Applicants' specification, *Wiley* indicates that the TWEAK receptor polypeptide plays a role in wound closure and angiogenesis. For example, antagonist TWEAK-Fc fusion polypeptides inhibited wound closure and angiogenesis *in vitro*. *See, Wiley* at pages 27-28 (Examples 3 & 4). And, also like Applicants' specification, Wiley indicates that antibodies directed against the TWEAK receptor may be useful for inhibiting tumor growth. *Compare Wiley* at page 31 (Example 6) *with Applicants' specification* at page 25, lines 22-24.

Hence, Applicants submit that the publication by *Wiley* lends third party corroboration of the specific and substantial utilities asserted in the present specification for the claimed polypeptides[1]; such as, for example, the specification's described utilities for the claimed polypeptides in detecting and/or treating vascular disorders, wound healing, and tumors (*e.g.* various carcinomas and malignant melanoma). Thus, Applicants submit that specific and substantial utilities have not only been asserted, but have also been independently corroborated. Applicants have herein canceled claim 11 without prejudice or disclaimer rendering rejection of this claim moot. And, Applicants respectfully request that the rejection of claims 25-76 under 35 U.S.C. § 101 be reconsidered and withdrawn.

Claim Rejections Under 35 U.S.C. § 112

a) Claims 11 and 25-76 were rejected under 35 U.S.C. § 112, first paragraph, on the basis that "since the claimed invention is not supported by either a specific or substantial asserted utility...one skilled in the art clearly would not know how to use the claimed

[1]Applicants note that the supportive evidence cited in *Wiley*, dated after the applicants' filing date, "can be used to substantiate any doubts as to asserted utility since it pertains to the accuracy of a statement already in the specification." *See e.g., In re Brana* 51 F.3d 1560, 1567 at n19 (Fed. Cir. 1995).

invention." *See*, Paper No. 11, page 5, last paragraph. Applicants have herein canceled claim 11 without prejudice or disclaimer rendering rejection of this claim moot. Moreover, based on the above provided explanations, Applicants submit that the present specification satisfies the statutory requirements under 35 U.S.C. § 101 for the pending claims. Accordingly, Applicants respectfully request that the corresponding rejection of claims 25-76 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Claim Rejections Under 35 U.S.C. § 112

b) Claims 11 and 37-76 were rejected under 35 U.S.C. § 112, first paragraph, as "allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." See, Paper No. 11, page 6, first paragraph. In particular, it was asserted "[t]hese Claims set forth variants and fragments of SEQ ID NO:59...[h]owever, no activity is provided for these variants and fragments...having 90% identity...there is no measurable function associated therewith." *See*, Paper No. 11, page 6, first paragraph.

Applicants have herein amended claims 37, 42, 47, 52, 57-58, 62-63, 67-68, and 72-73 (and thereby also dependent claims 38-41, 43-46, 48-51, 53-56, 59-61, 64-66, 69-71, and 74-76) to stipulate that the claimed polypeptides have a measurable functional activity wherein the polypeptides are capable of use in generating or selecting antibodies. Applicants have herein canceled claim 11 without prejudice or disclaimer rendering rejection of this claim moot. And, in view of the claim amendments made herein, Applicants respectfully request the rejection of claims 37-76 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Conclusion

Applicants respectfully request that the above-made amendment and remarks be entered and made of record in the file history of the instant application. The Examiner is

invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the examination of this application.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Date: July 26, 2002

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